DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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January 14, 2015

SIEMENS HEALTHCARE DIAGNOSTICS INC.
SARA KASTRUP
REGULATORY CLINICAL AFFAIRS SPECIALIST
511 BENEDICT AVENUE
TARRYTOWN NY 10591

Re: K143504
Trade/Device Name: IMMULITE® 2000 Albumin Calibration Verification Material,
IMMULITE® 2000 Myoglobin Calibration Verification Material
Regulation Number: 21 CFR 862.1660
Regulation Name: Quality control material (assayed and unassayed)
Regulatory Class: I, Reserved
Product Code: JJX
Dated: December 9, 2014
Received: December 10, 2014

Dear Ms. Sara Kastrup:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Stayce Beck -S

For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
*See PRA Statement below.*

510(k) Number *(if known)*

k143504

Device Name
IMMULITE® 2000 Albumin Calibration Verification Material (CVM)
IMMULITE® 2000 Myoglobin Calibration Verification Material (CVM)

Indications for Use *(Describe)*
The IMMULITE® Albumin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Albumin assay on the IMMULITE 2000 systems
The IMMULITE® Myoglobin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Myoglobin assay on the IMMULITE 2000 systems

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

**CONTINUE ON A SEPARATE PAGE IF NEEDED.**

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SIEMENS

# Section 006: 510(k) Summary

## 510(k) Summary

**Introduction:** According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

**The assigned 510(k) Number: _____**

| | |
|---|---|
| **1. Submitter** | |
| **Mailing Address:** | Siemens Healthcare Diagnostics Inc.<br>511 Benedict Avenue<br>Tarrytown, NY 10591 |
| **Contact Person:** | Sara Kastrup<br>Regulatory Clinical Affairs Specialist |
| **Phone Number:** | (914)-524-2317 |
| **Fax Number:** | (914)-524-2101 |
| **E-mail Address:** | sara.kastrup@siemens.com |
| **Date Prepared:** | December 9th, 2014 |
| **2. Device Name** | |
| **Proprietary Name:** | **IMMULITE® 2000 Albumin Calibration Verification Material** |
| **Measurand:** | Quality Control materials for IMMULITE® 2000 Albumin assay<br>Calibration Verification Material (CVM) for IMMULITE® 2000 |
| **Type of Test:** | Albumin assay |
| **Regulation Section:** | 21 CFR 862.1660, Quality Control Material |
| **Classification:** | Class I Reserved |
| **Products Code:** | JJX – Single (Specified) Analyte Controls (Assayed and Unassayed) |
| **Panel:** | Clinical Chemistry (75) |
| **3. Predicate Device Name** | IMMULITE® 2000 SHBG Calibration Verification Material (CVM) |
| **Predicate 510(k) No:** | K140541 |
| **4. Device Description:** | The Albumin Calibration Verification Material (CVM) contains one set of four vials each 2.0 mL after reconstitution. CVM1 contains bovine protein with preservatives. CVM2, CVM3 and CVM4 contain various levels of human albumin in a bovine protein matrix with preservatives. The CVMs are supplied in lyophilized form. |

| | |
|---|---|
| **5. Intended Use:**<br>**Indication for Use:** | See Indications for Use Statement below:<br>The IMMULITE® Albumin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Albumin assay on the IMMULITE 2000 systems. |
| **Special Conditions for Use Statement(s):** | For prescription use only |
| **Warnings and Precautions:** | Caution, potential biohazard<br>Contains human source material. Each donation of human blood or blood component was tested by FDA-approved methods for the presence of antibodies to human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) as well as for hepatitis B surface antigen (HBsAg) and antibody to hepatitis C virus (HCV). The test results were negative (not repeatedly reactive.). No test offers complete assurance that these or other infectious agents are absent; this material should be handled using good laboratory practices and universal precautions. |
| **Special Instrument Requirements:** | IMMULITE® 2000 Systems |
| **6. Technological Characteristics and Substantial Equivalence**<br>**Comparison with Predicate:** | A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® 2000 Albumin Calibration Verification Material (CVM) is substantially equivalent to the predicate device as summarized in **Table 1**. |

**Table 1:** Substantial Equivalence Comparison

| SIMILARITIES | | |
|---|---|---|
| | **Candidate Device IMMULITE 2000 Albumin CVM** | **Predicate Device IMMULITE 2000 SHBG CVM** |
| **Intended Use** | The IMMULITE® Albumin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Albumin assay on the IMMULITE 2000 systems. | The IMMULITE® SHBG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE SHBG assay on the IMMULITE 2000 systems. |
| **Form** | Lyophilized | Same |
| **Stability** | Stable unopened until the expiration date | Same |
| **Levels** | 4 | Same |
| **Use** | Single Use Only | Same |
| **Storage** | 2-8°C | Same |

| | DIFFERENCES | |
|---|---|---|
| | **Candidate Device IMMULITE 2000 Albumin CVM** | **Predicate Device IMMULITE 2000 SHBG CVM** |
| **Analyte** | Albumin | SHBG |
| **Matrix** | Bovine Protein with Preservatives | Buffered Bovine Protein with Preservatives |

## 7. Non-Clinical Performance Testing

Performance testing has been carried out to demonstrate that this device meets the performance specifications for its intended use. The following tests were performed on the candidate device.

### 7.1 Shelf Life Stability Summary:

The stability study was conducted to validate real-time shelf life claim for the IMMULITE 2000 Albumin Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM.
The IMMULITE® 2000 Albumin Calibration Verification Materials are stable up to 6 years when stored at 2-8°C prior to reconstitution.

#### 7.1.1 Shelf life Stability Protocol Summary:

The CVM study protocols are run as part of the calibrator stability testing. The stability CVMs and reference CVMs are run in duplicate (as a minimum) at the time points shown in **Table 2** and the dose value determined from the reference calibrator curve.

**Table 2:** Shelf life Stability Time Points

| CVM level | Time-Points (months) | | | |
|---|---|---|---|---|
| **LHACVM1** | 0 | 54 | 72 | 84 |
| **LHACVM2** | 0 | 54 | 72 | 84 |
| **LHACVM3** | 0 | 54 | 72 | 84 |
| **LHACVM4** | 0 | 54 | 72 | 84 |

#### 7.1.2 Shelf Life Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE Albumin requires dose value of stability calibrator/CVM to fall between ±10% of assigned dose for CVM level 2 and 3, and ±15% for CVM level 4. The acceptance criterion is summarized in **Table 3**.

**Table 3** Acceptance criteria for stability of IMMULITE 2000 Albumin CVM

| CVM level | Assigned Dose (µg/mL) | Guideline Criteria % difference to assigned dose | Acceptable dose range (µg/mL) | Review Limits |
|---|---|---|---|---|
| **LHACVM1** | 0.00 | Not Applicable | ≤ 2.5 | Controls are within 2SD of target on each curve |
| **LHACVM2** | 5.05 | ±10% | 4.55-5.56 | |
| **LHACVM3** | 20.7 | ±10% | 18.6-22.8 | |
| **LHACVM4** | 63.0 | ±15% | 53.6-72.5 | |

7.2 Open Vial Stability Summary:

The stability study was conducted to validate open component (in-use or open vial) shelf life and open component (in-use or open vial) claim for the IMMULITE 2000 Albumin Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms after reconstitution.

The IMMULITE® 2000 Albumin Calibration Verification Materials are stable up to 2 hours at ambient or room temperature (15-25°C) after reconstitution.

7.2.1 Open Vial Stability Protocol Summary:

The stability CVMs and reference CVMs are run in duplicate (as a minimum) at the time points shown in **Table 4** and the dose value determined from the on system 2-point adjustment.

**Table 4:** Open Vial Stability Time Points

| CVM level | Time-Points (hours) | | |
|---|---|---|---|
| **LHACVM1** | 0 | 2 | 6 |
| **LHACVM2** | 0 | 2 | 6 |
| **LHACVM3** | 0 | 2 | 6 |
| **LHACVM4** | 0 | 2 | 6 |

Using IMMULITE 2000 Albumin (L2KHA2) kit lot 236 Albumin CVM lot 092 was tested up to 6 hours at ambient or room temperature (15-25°C) conditions and compared to the determinations at time zero.

7.2.2 Open Vial Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE Albumin requires dose value of stability calibrator/CVM to fall between ±10% difference to the initial time point dose for CVM level 2 and 3, and ±15% to the initial time point does for CVM level 4. The acceptance criterion is summarized in **Table 5**.

**Table 5** Acceptance criteria for Open Vial stability of IMMULITE 2000 Albumin CVM

| CVM level | Assigned Dose (µg/mL) | Guideline Criteria % difference to initial time point | Acceptable dose range (µg/mL) | Review Limits |
|---|---|---|---|---|
| **LHACVM1** | 0.00 | Not Applicable | ≤ 2.5 | Controls are within 2SD of target on each curve |
| **LHACVM2** | 5.05 | ±10% | 4.55-5.56 | |
| **LHACVM3** | 20.7 | ±10% | 18.6-22.8 | |
| **LHACVM4** | 63.0 | ±15% | 53.6-72.5 | |

7.3 Traceability:

The IMMULITE Albumin CVMs are traceable to an internal material which has been gravimetrically prepared. The CVMs are manufactured using qualified materials and measurement procedures.

7.4 Value Assignment:

IMMULITE Albumin CVMs are 4 level materials which are a subset of 7 level Albumin calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of Albumin reagents and two point adjustors.

The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The assigned reference calibrators are prepared using Albumin antigen stock and are traceable to an internal material. Two levels of commercially available controls and 23 urine samples were used to validate calibrator/CVM value assignments.

The CVMs are manufactured using qualified materials and measurement procedures. The IMMULITE Albumin calibrators/CVMs were tested on 27 replicates in total, comprised of 9 runs, 3 replicates per run, 9 IMMULITE 2000 systems and 3 different reagent kit lots.The CVMs dose values are generated using the curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples and controls using the assigned CVM values. The controls must fall within their target ranges.

7.5 Expected Values/Reference Range:

Each CVM level was tested on tested on 27 replicates in total, comprised of 9 runs, 3 replicates per run, 9 IMMULITE 2000 systems and 3 different reagent kit lots. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2

Standard Deviation (SD). The expected values are provided in the IMMULITE® 2000 CVM Calibration Verification Material lot-specific package insert.

The expected assay range is 2.5-60 µg/mL. The target values in **Table 6** can be considered as guidelines.

**Table 6:** Target Values

| **Analyte target levels** | **CVM Level** | **Target Mean (µg/mL)** | **Standard Deviation (SD)** | **Target Range (µg/mL)** | |
|---|---|---|---|---|---|
| | LHACVM1 | 0.00 | - | 0.00 | 2.50 |
| | LHACVM2 | 5.05 | 0.38 | 4.29 | 5.81 |
| | LHACVM3 | 20.7 | 2.05 | 16.6 | 24.8 |
| | LHACVM4 | 63.0 | 6.0 | 51.0 | 75.0 |
| **Assay Range** | Up to 2.5-60µg/mL | | | | |

Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. The representative, total precision tabulated in the respective assay instructions for use may be considered as one factor when establishing local, acceptable ranges. The values provided above may be considered as guidelines. Value assignment is lot specific.

Standard/Guidance Documents Referenced**:**

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

Proposed Labeling**:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

## 8. Conclusion:

The IMMULITE® 2000 Albumin Calibration Verification Material is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the FDA cleared IMMULITE® 2000 SHBG Calibration Verification Material. The substantial equivalence of the device is supported by the non-clinical testing and was found to be comparable and supports the claims of substantial equivalence, product safety and effectiveness. Based on the testing completed and the comparisons with predicate device,

the IMMULITE® 2000 Albumin Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

SIEMENS

**510(k) Summary**

**Introduction:** According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.
**The assigned 510(k) Number: _____**

1. **Submitter**

| | |
|---|---|
| **Mailing Address:** | Siemens Healthcare Diagnostics Inc.<br>511 Benedict Avenue<br>Tarrytown, NY 10591 |
| **Contact Person:** | Sara Kastrup<br>Regulatory Clinical Affairs Specialist |
| **Phone Number:** | (914)-524-2317 |
| **Fax Number:** | (914)-524-2101 |
| **E-mail Address:** | sara.kastrup@siemens.com |
| **Date Prepared:** | December 9th, 2014 |

2. **Device Name**

| | |
|---|---|
| **Proprietary Name:** | **IMMULITE® 2000 Myoglobin Calibration Verification Material** |
| **Measurand:** | Quality Control material for IMMULITE® 2000 Myoglobin assay |
| **Type of Test:** | Calibration Verification Material (CVM) for IMMULITE® 2000 Myoglobin assay |
| **Regulation Section:** | 21 CFR 862.1660, Quality Control Material |
| **Classification:** | Class I Reserved |
| **Products Code:** | JJX – Single (Specified) Analyte Controls (Assayed and Unassayed) |
| **Panel:** | Clinical Chemistry (75) |

3. **Predicate Device Name**

| | |
|---|---|
| **Predicate 510(k) No:** | IMMULITE® 2000 Intact PTH Calibration Verification Material (CVM) K140258 |

4. **Device Description:** IMMULITE® 2000 Myoglobin Calibration Verification Material (CVM) contains one set of four vials each 2.0mL after reconstitution. CVM1 contains bovine serum with preservatives. CVM2, CVM3 and CVM4 contain various levels of human cardiac myoglobin in bovine serum with preservatives. The CVMs are supplied in lyophilized form.

5. **Intended Use:** See Indications for Use Statement below
**Indication for Use:** The IMMULITE® Myoglobin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Myoglobin assay on the IMMULITE 2000 systems.

| | |
|---|---|
| **Special Conditions for Use Statement(s):** | For prescription use only |
| **Warnings and Precautions:** | Caution, potential biohazard<br>Contains human source material. Each donation of human blood or blood component was tested by FDA-approved methods for the presence of antibodies to human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) as well as for hepatitis B surface antigen (HBsAg) and antibody to hepatitis C virus (HCV). The test results were negative (not repeatedly reactive.). No test offers complete assurance that these or other infectious agents are absent; this material should be handled using good laboratory practices and universal precautions. |
| **Special Instrument Requirements:** | IMMULITE® 2000 Systems |

| | |
|---|---|
| **6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:** | A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® Myoglobin Calibration Verification Material (CVM) is substantially equivalent to the predicate device as summarized in **Table 1**. |

**Table 1:** Substantial Equivalence Comparison

| SIMILARITIES | | |
|---|---|---|
| | **Candidate Device IMMULITE 2000 Myoglobin CVM** | **Predicate Device IMMULITE 2000 Intact PTH CVM** |
| **Intended Use** | The IMMULITE® Myoglobin Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Myoglobin assay on the IMMULITE 2000 systems | The IMMULITE® Intact PTH Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Intact PTH assay on the IMMULITE 2000 systems |
| **Storage** | ≤-20°C | Same |
| **Stability** | Stable unopened until the expiration date | Same |
| **Levels** | 4 | Same |
| **Use** | Single Use Only | Same |
| **Matrix** | Bovine Serum with preservatives | Same |
| **Form** | Lyophilized | Same |

| DIFFERENCES | | |
|---|---|---|
| | **Candidate Device IMMULITE 2000 Myoblobin CVM** | **Predicate Device IMMULITE 2000 Intact PTH CVM** |
| **Analyte** | Myoglobin | Intact PTH |

## 7. Non-Clinical Performance Testing

Performance testing has been carried out to demonstrate that this device meets the performance specifications for its intended use. The following tests were performed on the candidate device.

### 7.1 Shelf life Stability Summary:

The stability study was conducted to validate shelf life claim for the IMMULITE 2000 Myoglobin Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM before and after reconstitution.

The Myoglobin Calibration Verification Materials are stable up to 7 years when stored at -20°C.

#### 7.1.1 Shelf life Stability Protocol Summary:

The CVM study protocols are run as part of the calibrator stability testing. The stability CVMs and reference CVMs are run in duplicate (as a minimum) at the time points shown in **Table 2** and the dose value determined from the reference calibrator curve.

**Table 2:** Shelf life Stability Time Points

| CVM Level | Time-Points (months) | | | |
|---|---|---|---|---|
| **LMYCVM1** | 0 | 54 | 60 | 84 |
| **LMYCVM2** | 0 | 54 | 60 | 84 |
| **LMYCVM3** | 0 | 54 | 60 | 84 |
| **LMYCVM4** | 0 | 54 | 60 | 84 |

#### 7.1.2 Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE Myoglobin criteria requires dose value of stability calibrator/CVM to fall between ±10% of assigned dose for CVM level 2, 3, and 4.

The acceptance criterion is summarized in **Table 3**.

**Table 3** Acceptance criteria for stability of IMMULITE 2000 Myoglobin CVM

| CVM level | Assigned Dose (ng/mL) | Guideline Criteria % difference to assigned dose | Acceptable dose range (ng/mL) |
|---|---|---|---|
| **LMYCVM1** | **0.00** | **N/A** | **≤ 2.0** |
| **LMYCVM2** | **26.6** | **±10%** | **23.9-29.3** |
| **LMYCVM3** | **116** | **±10%** | **104-128** |
| **LMYCVM4** | **1050** | **±10%** | **945-1155** |

7.2 Open Vial Stability Summary**:**

The stability study was conducted to validate the open component (in-use or open vial) for the IMMULITE 2000 Myoglobin Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms after reconstitution.

The Myoglobin Calibration Verification Materials are stable up to 8 hours after reconstitution.

7.2.1 Open Vial Stability Protocol Summary:

The stability CVMs and reference CVMs are run in duplicate (as a minimum) at the time points shown in **Table 4** and the dose value determined from the on system 2-point adjustment.

**Table 4:** Open Vial Stability Time Points

| CVM Level | Time-Points (hours) | | | | | |
|---|---|---|---|---|---|---|
| **LMYCVM1** | 0 | 2 | 4 | 6 | 8 | 9 |
| **LMYCVM2** | 0 | 2 | 4 | 6 | 8 | 9 |
| **LMYCVM3** | 0 | 2 | 4 | 6 | 8 | 9 |
| **LMYCVM4** | 0 | 2 | 4 | 6 | 8 | 9 |

7.2.2 Open Vial Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE Myoglobin criteria requires dose value of stability calibrator/CVM to fall between ±10% difference to the initial time point dose for CVM level 2, 3, and 4.

The acceptance criterion is summarized in **Table 5**.

**Table 5** Acceptance criteria for open vial stability of IMMULITE 2000 Myoglobin CVM

| CVM level | Assigned Dose (ng/mL) | Guideline Criteria % difference to initial time point | Acceptable dose range (ng/mL) |
|---|---|---|---|
| **LMYCVM1** | **0.00** | **N/A** | **≤ 2.0** |
| **LMYCVM2** | **26.6** | **±10%** | **23.9-29.3** |
| **LMYCVM3** | **116** | **±10%** | **104-128** |
| **LMYCVM4** | **1050** | **±10%** | **945-1155** |

7.3 Traceability:
The IMMULITE Myoglobin CVMs are traceable to an internal standard. The CVMs are manufactured using qualified materials and measurement procedures.

7.4 Value Assignment:
The Myoglobin CVMs are 4 level materials which are a subset of 10 level Myoglobin calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of Myoglobin reagents and two point adjustors.

The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The assigned reference calibrators are prepared using Myoglobin antigen stock and are traceable to an internal standard. Three levels of commercially available controls and 30 samples (25 spiked samples and 5 normal samples) were used to validate calibrator/CVM value assignments.

The calibrators/CVMs are manufactured using qualified materials and measurement procedures. The calibrators/CVMs were tested on 15 replicates in total, comprised of 5 runs, 3 replicates per run, 3 IMMULITE 2000 systems and 4 different reagent kit lots. The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples, spiked patient samples and controls using the assigned CVM values. The controls must fall within their target ranges.

7.5 Expected Values/Reference Range:
Each CVM level was on 15 replicates in total, comprised of 5 runs, 3 replicates per run, 3 IMMULITE 2000 systems and 4 different reagent kit lots. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The expected values are provided in the IMMULITE® 2000 Myoglobin CVM Calibration Verification Material lot-specific package insert.

The expected assay range is up to 1000 ng/mL. The target values in **Table 6** can be considered as guidelines.

**Table 6:** Target Values

| Analyte target levels | CVM Level | Target Mean (ng/mL) | Standard Deviation (SD) | Target Range (ng/mL)n | |
|---|---|---|---|---|---|
| | LMYCVM1 | 0.00 | - | 0.00 | ≤2.0 |
| | LMYCVM2 | 27.7 | 1.5 | 24.7 | 30.7 |
| | LMYCVM3 | 123 | 7.0 | 109 | 137 |
| | LMYCVM4 | 999 | 70 | 859 | 1139 |
| **Assay Range** | Up to 1000 ng /mL | | | | |

Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. The representative, total precision tabulated in the respective assay instructions for use may be considered as one factor when establishing local, acceptable ranges. The values provided above may be considered as guidelines. Value assignment is lot specific.

Standard/Guidance Documents Referenced**:**

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

Proposed Labeling**:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

## 8. Conclusion:

The IMMULITE® 2000 Myoglobin Calibration Verification Material is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the FDA cleared IMMULITE® 2000 Intact PTH Calibration Verification Material. The substantial equivalence of the device is supported by the non-clinical testing and was found to be comparable and supports the claims of substantial equivalence, product safety and effectiveness. Based on the testing completed and the comparisons with predicate device, the IMMULITE® 2000 Myoglobin Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.